Replacement Sheet
Sheet 1 of 14
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2123
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)



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_	·	NASTER PROCESS PARAM	eters ta	BLE-BLOPHARMACEUTICAL	
l			Group	1	
L	Unit Operation Type	Parameter	Soln.	·	Parameter
Ť	i Inoculum Prep	Number of Flasks Hedia Volume/Flask		0.25 liters	Temperature Agitation Duration
17	Flask Growth	Scale Up Ratio Media Volume/Flask		10 Fold 1.25 L	Temperature Agitation Duration
T3	Production	Scale Up Ratio Fermentor Yorking Volume Antifoam A Antifoam B Base Acid	S-101 S-102 S-103 S-104 S-105	10 Fold 500 Liters 1 MI/L 1 MI/L 5 MI/L 5 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
14		Number of Ampules Volume Per Ampule Starting Cell Density Ampule Split Ratio Culture Vessel Type Feed Volume	. 0 233	2 HI 300,000 Cells/HI 1 Vessels/Ampule Rull. Bot. 100 HI	Serum Content Feed Rate Days to Confluence
5	Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		RB 100 MI 2.0% Fetal Bovine Serus	Feed Rate Days to Confluence
	Spinner Flask Seeding	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Mumber of Media Washes No.of Media/Serum Washes		(Liters 0.1 L Cells/L Flask 5 Ga/Liter 2 2 2 FBS	Serum Content Feed Rate Days to Confluence
	Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Food Volume		500 Liters 8.3 5 Ga/Liter 2	Serum Content Feed Rate Days to Confluence Serum Free Media Vashes
	Biosynthesis Bioreactor Preparation Utollow Fiber Reactor)	Reactor Feed Volume Kumber of PBS Vashes Kumber of Media Vashes No. of Nedia/Serum Vashes Serum Content		100 Liters 2 2 2 2.0% Fetal Bovine Serun	Number of Reactors Feed Rate Days to Confluence
	Biosynthesis Bioreactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of P85 Washes Number of Nedia Vashes No.of Media/Serum Washes Serum Content		Liters Gas/L	Number of Reactors Feed Rate Days to Confluence
]	initial seeding	Number of Appules Volume Per Appule Starting Cell Density Appule Split Ratio		2 2 MI 300,000 Cells/MI 1 Vessels/Ampule	Serva Content Feed Rate Oays to Confluence

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1	6conb	2	Group 3				
}_	Soln.		Parameter	Soln.			
/		37 C 200 RPM 18 Hours	Final 00		12		
\		37 C 200 Hours 18 RPM	Final OD		12		
		37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD Dry Cell Mass Product Concentration CIP		9.96 Gas TDCM/L 0.3 Gas Product/L Y		
		2.0% Fetal Bovine Serua 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%		
		1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%		
		2.0% Fetal Bovine Serus 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%		
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.		2500% Ng Prod/L 0.125 Ng TP/MI		
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/NI		
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Ng Prod/L 0.125 Ng TP/HI		
		2.0% Fetal Boyine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%		

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HASTER PROCESS PARAMETERS TARILE-RI OCHARMACEUTETCAL

No. of Predia/Serum Washes 2 1 1 1 1 1 1 1 1 1		HASTER PROCESS PARA	HETERS T	ABLE-BLOPHARNACEUTICAL	
Culture Vessel Split (Vessel Split Ratio Feed Volume Vessel Split Ratio German Content (Vessel Split Ratio German Content) 12 Splinner Flask Split (Vessel Split Ratio German Content) 12 Splinner Flask Split (Vessel Split Ratio German Content) 13 Blosynthesis (Vessel Flask Ratio German Content) 13 Blosynthesis (Vessel Flask Ratio German Content) 14 Cities (Vessel Flask Ratio German Content) 15 Geniter (Vessel Flask Ratio German Content) 16 German Content Feed Rate (Vessel Flask Ratio German Content) 18 Blosynthesis (Vessel Type Feed Volume Vessel Flask Ratio German Content) 19 German Content Feed Rate (Vessel Flask Ratio German Content) 10 German Content Feed Rate (Vessel Flask Ratio German Ratio German Content) 10 German Content Feed Rate (Vessel Flask Ratio German Ratio German Feed Rate (Vessel Flask Ratio German Ratio German Content) 10 German Content Feed Rate (Vessel Ratio German Rati			Group	i	
Spinner Flask Split Flask Feed Volume Serum Content Se	Unit Operation Type	Parameter	Soln.		Parameter
12 Spinner Flask Split Flask Feed Volume Vessel/Flask flatio UCarrier Density Rumber of PRS Vashes Humber of PRS Vashes Humber of Redia Vashes Bioreactor Preparation Spinner/Reactor Ratio Usarrier Density Rumber of Redia Vashes Bioreactor Preparation Spinner/Reactor Ratio Usarrier Density Rumber of Redia Vashes Bioreactor Preparation Usarrier Density Rumber of Redia Vashes Bioreactor Preparation Usarrier Density Flatk Feed Volume Usarrier Density Rumber of PRS Vashes Rumber of Redia Vashes So. of Redia/Serum Vashes Spinner/Reactor Ratio UCarrier Density Rumber of Redia Vashes So. of Redia/Serum Vashes Spinner/Reactor Ratio Carrier Density Rumber of Redia Vashes No. of Redia/Serum Vashes Spinner/Reactor Ratio Carrier Density Rumber of Redia Vashes No. of Redia/Serum Vashes Spinner/Reactor Ratio Carrier Density Rumber of Redia Vashes No. of Redia/Serum Vashes Serum Content Feed Rate 2 Days to Confluence Days to Confluence 3 Serum Content Feed Rate 0.1 L Cells/L Flask Serum Content Feed Rate Days to Confluence 0.1 L Cells/L Flask Serum Content Feed Rate Days to Confluence 1 Serum Content Feed Rate Days to Confluence 2 Days to Confluence Days to Confluence 2 Days to Confluence 3 Days to Confluence 4 Days to Confluence 2 Days to Confluence 2 Days to Confluence 3 Days to Confluence 4 Days to Confluence 4 Days to Confluence 5 Days to Confluence 5 Days to Confluence 5 Days to Confluence 5 Days to Confluence 6 Days to Confluence		Feed Valume		100 MI	Trypsin Wash
Vessel/Flask Ratio Utarrier Density Humber of PRS Vashes Some Preparation Spinner/Pacator Ratio Utarrier Density Some Preparation Utarrier Density Some Preparation Utarrier Density Some Preparation Utarrier Density Some Preparation Utarrier Density Utarrier Density Humber of PRS Vashes		1		R8 100 KI	Days to Confluence PBS Vashes
13Blosynthesis Reactor Feed Volume Spinner/Reactor Ratio Utarrier Density Number of PRS Vashes Number		Vessel/Flask Ratio uCarrier Density Humber of PBS Washes Humber of Media Washes No. of Media/Serum Washes		0.1 L Cells/L Flask	Feed Rate
Confidence Con		Number of PBS Washes Number of Media Washes		8.3	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
SIntial Coupling Flask Feed Volume	a ratorice oca receivi	Reactor Feed Volume uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes ISerum Content			Feed Rate
Spinner/Reactor Hatto UCarrier Density Number of PBS Washes Seven Free Rate Days to Confluence Serum Free Redia Washes Serum Free Redi	, ,	Flask Feed Volume		0.1 L Cells/L Flask 5 Ga/Liter 2 1	Feed Rate
Reactor Feed Volume 100 Liters Number of Reactors 100 Liters		Springer Heactor Hatto uCarrier Density Number of PBS Washes Number of Hedia Washes No of Hedia/Serum Washes			
Environmental Temperature Thav Duration Homogenization Crude Product Yield Liquid/Solid Ratio Homogenization Temp Homogenization Temp Homogenizer Type Energy Input Durating Environmental Temperature 16 Hours 25 C 16 Hours	7Peptide Cleavage	Reactor Feed Volume Number of PBS Vashes Number of Hedia Vashes No.of Hedia/Serum Vashes		222	Feed Rate
Liquid/Solid Ratio Homogenization Temp. Homogenizer Type Energy Input Duration A C L Solution/Kg Tissue 10 L Solution/Kg Tissue 200 HP/100L/Hr Homogenizer Type 200 HP/100L/Hr	1 1	Environmental Temperature	2	5 Ga Crude Prod./Kg Tissue 25 C 16 Hours	Contaminant Protein Conc
Liquid Thawing	- 8	Crude Product Yield Liquid/Solid Ratio loanogenization Temp. loanogenizer Type nergy Input kration	25	10 L Solution/Kg Tissue A C RS 200 HP/100L/Hr	Contaminant Protein Conc.
	Liquid Thawing			7 1001 5	

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Group	2		Group 3	-
Soln.		Parameter	Soln.	
	200 MI 100 MĪ			
	1 Feed per vessel per 2 Days 2 Days 200 HI 100 HI	Amplification Factor		100%
	2.0% Fetal Bovine Serua 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
	2.0% Fetal Bovine Serus 1 Feed per vessel per 2 Days 10 Days 2 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
	1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Hg Prod/L 0.125 Hg TP/HI
·	2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
	2.0% Fetal Bovine Serus 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.		2500% Ng Prad/L 0.125 Ng TP/HI
	1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
	100 Gm/L	Temperature Regulation CIP SIP	Ÿ	
	100 Ga/ L	Temperature Regulation CIP SIP	Y	
		Applification Factor		100%

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MACTED DOOCEC DADANCTEDO TADAS DI COMMUNICACISTAMA

_		MASTER PROCESS PARA	AKETERS TAB	LE-BLOPHARHACEUTIC	AL .
ı			Group 1	, .	·
_	Unit Operation Type	Parameter	Soln.		Parameter
12	Product Ppt by Solids	Reagent Concentration		· 1H	Kgms of Reagent/Liters Produ Temperature Addition Time Additional Mix Time
2	Product Ppt by Liquids	Reagent Concentration		1 K	Liters Reagent/Liters Produc Temperature Addition Time Additional Mix Time
23	Contaminant Ppt by Solids	Reagent Concentration		1 H	Kows of Reagent/Liters Produ Temperature Addition Time Additional Mix Time
24	Contaminant Ppt by Liquids	Reagent Concentration		1 M	Liters Reagent/Liters Produc Temperature Addition Time Additional Mix Time
5	Solids Harvest Tangential Flow NF	Porosity Average Flux Rate Total Throughout Filtration Time		0.2 Kicron 11 L/SF/HR at 40 Psig at 4 C 400 Liters/SF	Flush Prime Concentration Factor Wash Regenerate
B	Continuous Centrilugation Solids Harvest	System Void Volume		1 HR 5 Liters	Store RCF Tine Yolume Reduction Vash Volume
	Continuous Centrifugation Supematant Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
	Dilution	System Vold Volume	·	6 Liters	RCF Time Yolune Reduction Wash Volume
ES	laich Centrifugation loilds Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume

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	Group	2	Group 3				
\sum	Soln.		Parameter	Soln.	·		
$\langle -$							
/- }		0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y		
-		0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of I.P. Temperature Regulation CIP SIP		95% 95% Y		
)	-	0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y		
		0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y		
		2 L/SF 2 L/SF 10 Fold 0.5 L/SF 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of T.P. Teaperature Regulation CIP SIP		95% 95% Y Y		
		10,000 X 6 50 Minutes 30 X Vol. Reduction 0.2 X System Vold Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95X 95X Y Y		
		10,000 X G 30 Minutes 0.062 X Yol. Reduction 1.5 X System Vold Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		85% 0.3		
		10,000 X 6 30 Minutes 16 X Vol. Reduction 1.5 X System Vold Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95		
	·	10,000 X 6 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP		95% 0.95		

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			Group	1	
L	Unit Operation Type	Parameter	Soln.		Parameter
13	Batch Centrifugation Supematent Harvest	System Vold Volume		6 Liters	RCF Time Volume Reduction Wash Volume
31	Cell Disruption High Press. Homogen.	Product Temperature Utility Temperature Void Volume		B C 2 C 5 Liter	Number of Passes Pressure Flow Rate Temperature Increase
3 2	Cell Disruption Bead Hill	Number of Passes Bead Size Yold Yolune Flow Rate		0.5 LPH	
33	Cell Disruption Chemical Lysis	Reagent Temperature Exposure Time		0.5 M NaOH 4 C 2 Hours	Liters Reagent/Ga Produ Titration
34	Microfiltration Tangential Flow	Porosity Average Flux Rate Total Throughout		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF	Flush Prime Vash Solids ikeoenerate
S	Microfiltration Dead End	Total Throughput Filtration Time Porosity Average Flux Rate Total Throughput		2 IR 0.2 Hicron 50 L/SF/IR at 40 Psig at 4 C 400 Liters/SF	Store Flush Prime Vash Solids Reggereste
di G	Jitrafiltration concentration/Dilution	Filtration Time		0.5 HR 60 K MML 3 L/SF/RR at 40 Psig at 4 C 2 HR	Store Flush Prime Wash Dilute Concentrate Solids
	lov Dialysis	Porosity Average Flux Rate Dialysis Time		60 K NMA 3 L/SF/HR at 40 Psig at 4 C 2 HR	Regenerate Flush Prime Dialysis Buffer Wash Solids
PH	rod .Ads .Chronatography PLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity	1	100 Cm/Hr at 45 Psig and	Regenerate Column Equilibration Column Vash Column Elute A Column Elute B Column Regenerate Column Regenerate
PM	rod.Ads.Chromatography LC	Column Capacity Column Oversize Factor	1	O NG Prod./HI Of Packing	Column Store Column Equilibration Column Wash

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			522 LYHANE IEHS TARIFE-RICHHAI	AMCEUIT	AL			
_	6comb	2		Group 3				
	Soln.		Parameter	Soin.				
⊬	 		SIP		v			
-	 	10,000 XG		ļ	Y			
		30 Minutes 16 X Vol.Reduction	Step Recovery of Product Step Recovery of T.P.		95% 0.95			
L		1.5 X System Vold Volume	Temperature Regulation CIP SIP		Y Y Y			
		6 Times 12,000 PSI 5 LPH	Rinse Step Recovery of Product Step Recovery of T.P.		500% Vold Volumes 95% 95%			
		1.8 Degrees C/1,000 PSI	SIP .		Y Y Y			
		,	Step Recovery of Product Step Recovery of T.P.	·	95%			
			Temperature Regulation CIP SIP		Y			
		0.4 L/Ga 0 HI/Liter	Step Recovery of Product Step Recovery of T.P.		95%			
			Teaperature Regulation CIP SIP		Y			
		2.00 L/SF 2.00 L/SF 0.50 L/SF	Step Recovery of Product Step Recovery of T.P.		95% 95%			
		0.30% Of Product Solution 1.00 L/SF 2.00 L/SF	Temperature Regulation CIP SIP		Y Y Y			
		0 L/SF 0 L/SF 0.50 L/SF	Step Recovery of Product Step Recovery of T.P.		95% 0.95%			
		0.003 Of Product Solution 1 L/SF 2 L/SF	CIP SIP		N N N			
		2.00 L/SF 2.00 L/SF 0.50 L/SF 10.0 Fold	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation		2.00 L/SF 95% 95% 95%			
_	\bot	0.30% Of Product Solution 1.00 L/SF	CIP SIP Store		1 1			
		2 L/SF 2.00 L/SF 5.0 X Feed Stream Volume	Step Recovery of Product Step Recovery of T.P.		200% L/SF 95% 95%			
_		0.50 L/SF 0.30% Of Product Solution 1.00 L/SF	Temperature Regulation CIP SIP					
		5 Column Volumes 3 Column Volumes 3 Column Volumes	Prod.Elution Volume Step Recovery of Product Step Recovery of T.P.		80% 95% 95%			
		O Column Volumes 1 Column Volumes 2 Column Volumes	Temperature Regulation CIP SIP					
F		5 Column Volumes 3 Column Volumes	Prod.Elution Volume Step Recovery of Product		80% 95%			

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r		NASIEN PHOLESS PANALE	ILUS IND	LE-BLUITIANNAUEUI ICAL	
-					
-	Unit Operation Type	Parameter	Soln.		Parameter
	·	Column Aspect Ratio Max. Linear Velocity		0.37 H/D 100 Ca/Hr at 45 Psig and 4 C	Column Elute A Column Elute B Column Regenerate Column Store
	40 Prod .Ads .Chromatography LPLC	Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./M1 Of Packin 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	g Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
	11 Cont .Ads .Chroaatography HPLC	Column Oversize Factor Column Aspect Ratio Max. Linear Velocity	·	30 NG Cont./MI Of Packin 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4.6	Column Equilibration Column Mash Column Elute A Column Elute B Column Regenerate Column Store
	2 Cont .Ads.Chroaatography MPLC	Column Aspect Hallo Max. Linear Velocity		10 MG Cont./MI Of Packin 1.5 Fold 0.37 H/D 100 Cn/Hr at 45 Psig and 400% C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
	3 Cont. Ads. Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 KG Cont /M1 Of Packing 1.5 Fold 0.37 H/D 100 Cn/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Elute B Column Stare
	Size Excl. Chronatography HPLC	Load Capacity Length Hax. Linear Velocity Void Volume	.5	X of Total Column Yolume 100 Cm 100 Cm/fir at 45 Psig and 4 C 25X Column Yolume	Column Equilibration Column Wash Column Regenerate Column Store
	Size Excl. Chronatography HPLC	Load Capacity Length Max. Linear Velocity Void Volume	5	X of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
	Size Excl.Chromatography LPLC	Load Capacity Length Max. Linear Velocity Yoid Volume	9	Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
	Dilution ·	Dilution Factor		3 Liters/Liter	Dilution Time Additional Mix Time
T48	Resolubilization F	leagent/Product Ratio		0 L/Kg Product	Reagent 1 Concentration
1	Į,	issolution Tine dditional Hix Tine	-	0.50 Hours 0.50 Hours	/

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		SS PARAMETERS TABLE-BLOPHARM	ACEUTICAL			
Group		Group 3				
Soln	.	Parameter	Soln.			
	3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Step Recovery of T.P. Temperature Regulation CIP SIP		95% N Y		
	5 Column Yolunes 3 Column Yolunes 3 Column Yolunes 2 Column Yolunes 1 Column Yolunes 2 Column Yolunes	Prod. Elution Voluce Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% 95% 95% N Y		
	5 Column Yolumes 3 Column Yolumes 3 Column Yolumes 2 Column Yolumes 1 Column Yolumes 2 Column Yolumes	Prod. Elution Yoluxe Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% 95% 95% 95% N		
	5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Iemperature Regulation CIP SIP		42% 95% 95% 95% Y		
	5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95% 95% N Y		
	4 Coluan Yolunes 1 Coluan Yolunes 1 Coluan Yolunes 2 Coluan Yolunes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Iemperature Regulation CIP SIP		42% Columns Volumes 95% 95%		
)	4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		42% Columns Volumes 95% 95%		
	4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	l.	42% Columns Volumes 95% 95%		
	0.5 Hours 1 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	Y	95% 95%		
	Vater Dist.	Step Recovery of Product Step Recovery of T.P.		95% 95%		
		leaperature Regulation CIP SIP	ĮŸ			

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		,			VOLT-OF A INABMOED LEVE	
		·		Group	1.	
1		Unit Operation Type	Parageter	Soln.		Parameter
	49	Enzymatic Modificatio	nEnzyme to Product Ratio Enzyme Concentration Reaction Temp Reaction Duration		0.084 Liters of Enzyme Stock Per Liter of Start Proc. Vol. 2 Mg/MI 37 Degrees C 30 Minutes 100%	Titration Solution-1 Titration Solution-2 Neutralization
	50	Lyophilization	Product Capacity/Load Product Unit Size	<u></u> .	8 Units 100 Grams/Unit	Lyophilization Time Product Weight Reduction
ŗ	51	Heat Exchange	Process Initial Temp. Process Final Temp Utility Initial Temp. Utility Final Temp. Process Specific Heat Design Type(P.I.C)		98.6 Degrees C 39.2 Degrees C 34 Degree C 5 Degrees C 38.6 K BTV/Hr	Exposure Tine
15	25	Storage	cesign Typeur.1.07		P	
	S		Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid		50 Liters 1 MI/L 1 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
			Flask Feed Volume Spinner Split Ratio utarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serun Washes		5 Ga/Liter	Serum Content Feed Rate Days to Confluence
55	G		Flask Feed Volume Spinner Solit Ratio Carrier Density Cumber of PBS Vashes Cumber of Hedia Vashes Oo, of Hedia/Serum Vashes		5 Ga/Liter	Serum Content Feed Rate Days to Confluence
56	a	lture Flask Split	O. OF TRUSH OF THE ROSIES		C 1 D3	. (
7	St	irred Tank Reactor				
8	FI	uldized Bed Reactor P P U	rocess Initial Temp. rocess Final Temp tility Initial Temp		37 Degree C 4 Degree C 2 Degree C	xposure Time

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Γ	Group 2		Group 3					
\vdash	Soln.		Propertos	Parameter Soln.				
<i>[</i>	00111.		rai diletei	301R.				
		0.067 L/L Process 0.02 L/L Process 0.57 L/L Process	Step Recovery of Product Step Recovery of T.P.		95% 95%			
			Tenperature Regulation CIP SIP		Y Y			
		18 Hours 0.95	Step Recovery of Product Step Recovery of T.P.		95% 95%			
			CIP SIP		Y Y Y			
		1 Hours	Step Recovery of Product Step Recovery of T.P.		100% 100%			
			Teoperature Regulation CIP SIP		Y Y Y			
			Step Recovery of Product Step Recovery of T.P.		95% 95%			
			Tenperature Regulation CIP SIP		Y Y			
		37 Hours 1 HP/100L 1.5 YYH 5 PSIG 21 Hrs	Final OD CIP		12 Y			
		2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1			
1		2% FBS	Amplification Factor		1			
		1 Feed per vessel per 2 Days 2 Days						
+	\dashv		Step Recovery of Product		A QS			
		•	Step Recovery of Product Step Recovery of T.P.		0.95 95% Y			
		-	CIP SIP		1			
1		50% Hours	Step Recovery of Product Step Recovery of T.P.	1	0.95 100%			

Replacement Sheet
Sheet 13 of 14
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.0020004; Group Unit: 2123
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: Method for Scheduling Solution Preparation in
Biopharmaceutical Batch Process Manufacturing
(As Amended)

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_				EL-OCU INTENACOTION.	
ļ		Group 1			
L	Unit Operation Type	Parameter	Soin.		Parameter
-		Utility Final Teap. Process Specific Heat Design Type(P.T.C)		5 Degrees C 12 K BTV/Hr	
59	Liquid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Addition Duration Additional Mix Duration Mix Energy		1 L Extraction/L Product 4 C 0.5 Hours 4 Hours 0.3 HP/100 L	Phase Separation Time / Product Phase (Top/Botton Harvest Time
60		Liquid/Liquid Ratio Extraction Temperature Duration Hix Energy		1 L Extraction/L Product 4 C 4 Hours 0.3 HP/100 L	Phase Separation Time / Product Phase(Top/Bottom Harvest Time
OU		Extraction Temperature Duration		4 C 4 Hours	Phase Se Product Harvest

Replacement Sheet
Sheet 14 of 14
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	Group 2			Group :	3
_	Soln.		Parameter	Soln.	
· }			Temperature Regulation CIP SIP		Å
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50% Y
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50%

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